

HORMONAL

(PERISTALTIC HORMON)

According to Dr. Zuelzer.

Constipation



WITH COMPLIMENTS.

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E. Schering)

IN, GERMANY.

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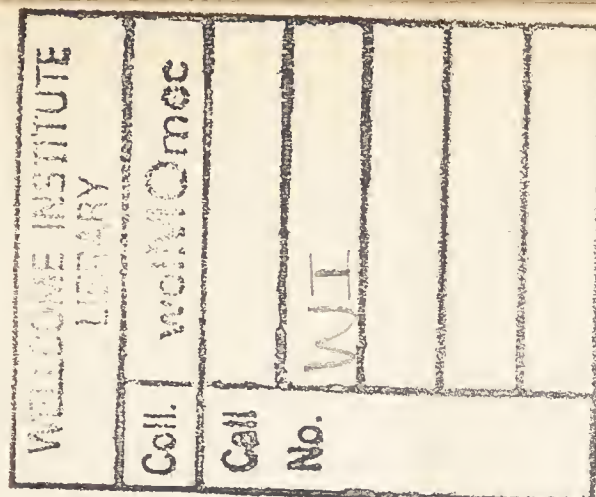
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HORMONAL

(PERISTALTIC HORMON)

According to Dr. Zuelzer.

Normal intestinal peristalsis is caused, according to the observation of Zuelzer, Dohrn and Marxer, by a specific cell product (Hormon), which appears to be chiefly stored in the spleen. This cell product is now prepared under Royal letters patent and introduced into therapy by Messrs Schering, of Berlin, under the trade name of

HORMONAL,

in bottles containing 20 c.cm. in a perfectly sterile condition. Prior to leaving the works, its peristaltic effect is tested on animals. When injected direct into the blood circulation of the trial animal, an effective preparation produces, within a few seconds, a very strong peristaltic wave, commencing at the duodenum and proceeding to the rectum, followed by discharge of faeces and gas from the anus. (Clinical.)

Hormonal, in the first instance, is indicated in the various forms of chronic constipation, where success, by the application of the usual methods, has not been permanently obtained, or has entirely failed. In consequence of its specific action, Hormonal cannot be classified with other laxatives. It surpasses these in the fact that it induces intestinal peristalsis in the *physiological sense*, and the effect in those cases which react to the treatment is lasting. Constipations which

have existed for years and resisted every other treatment are in most cases overcome by a single injection of Hormonal, the normal intestinal peristalsis is rearranged and evacuation takes place regularly for several weeks and even months. It is as though a stationary pendulum, by a single push, had again taken up its action (Dr. Saar). The effect frequently becomes permanent after second, third or later injection. As already mentioned, all cases do not react to Hormonal. It cannot yet be said which cases of constipation are best suited for the Hormonal treatment.

In intestinal atony (Crämer), Hormonal has proved generally good. Hormonal is further indicated in the ileo post-operative and peritonitic intestinal paralysis. In such intestinal paralysis, Hormonal is often the means of saving the patient's life. The prophylactic application of Hormonal might be of good service in abdominal operations.

APPLICATION AND DOSE.

In chronic constipation, should be injected intramuscularly. In acute intestinal paralysis, intravenously.

Hormonal is supplied for intramuscular injections (in amber bottles) and for intravenous injections (in blue bottles), each containing 20 cc. The preparation for intramuscular injection contains an addition of 0.25% Beta Eucaine hydrochloride. The intravenous injection is free from Eucaine. Both kinds of Hormonal contain 0.4% Trikresol as a preservative.

Dose :—For adults, the quantity to be injected varies from 15-20 cc. according to the severity of the case. This applies to both kinds of Hormonal. Children are given proportionately less. Prof. Henle used in a baby of four months 1 cc., and in a boy of seven years 12 cc., in both cases with success.

By intramuscular injection :—Introduce one half of the dose into the right and the other into the left gluteal

muscles. The injection should be carried out very slowly and under aseptic conditions. It is necessary to use a needle of sufficient length, in men 8 to 10 c.cm. (3 to 4 inches), in women, 10 to 12 c.cm. (4 to 4½ inches), to insure that the injection is made into the muscle; if introduced into the ordinary fatty tissues of the buttock, some 6 c.cm. (2½ inches) thick, sometimes painful effects are produced. Should severe pains set in during the injection, one has undoubtedly entered into a myalgic centre, and it is advisable to inject elsewhere. The muscles of the outside of thigh are very suitable. On the day of injection, it is advisable to give a purgative, e.g. two tablespoonfuls of Castor Oil, in order to dislodge any large fæces that may be in the intestines. Experience shows that a temporary rise of temperature occurs almost regularly, consequently Dr. Saar recommends carrying out the injection in the early morning, and keeping the patient in bed during the day to enable the temperature to become normal before night. To prevent recurrence of the old trouble after successful motion, prophylactic measures must be taken, viz. suitable diet, advice for regularity in motion, strengthening the abdominal muscles, etc.,

By intravenous injection:—The intravenous injection is best carried out, subject to the usual carefulness, into the arm vein at the elbow. During the treatment with Hormonal, the application of Morphia is to be avoided, as thereby its action is influenced. According to present observations Hormonal injections remain efficacious at least eight months.

It is advisable always to mention distinctly which kind of Hormonal is required, whether intramuscular or intravenous.

STIMULATION OF THE PERISTALTIC ACTION OF THE INTESTINE BY INTRAVENOUS INJECTION OF "PERISTALTIC HORMONS."*

By G. ZUELZER, in collaboration with MAX DOHRN
and ANTON MARXER, Berlin.†

BIOLOGICAL investigation during recent years has taught us that the varying influence of the functions of different organs upon each other is not exerted through the agency of the nervous system. It is found, on the contrary, that in the individual organs certain chemical substances are formed in metabolism which are transported by means of the circulation to more remote organs and are there capable of exerting quite a different action. It is these substances, therefore, as was first pointed out by the English physiologist Starling,‡ which are calculated to excite certain cell groups to certain definite functions. These substances are to be described as irritants, in contrast to the nutritive substances. For these reasons Starling designates the substances as "hormons" (from the Greek, *δρμάω* = I excite, or stimulate). As an example, the Mamma hormon discovered by Starling may be taken. It is well known that from the beginning of gravidity and during the entire period of pregnancy a constantly increasing growth of the breast glands takes place. It might have been supposed that this growth must stand in some causal connection with the change in the ovaries, the placenta, the uterine mucous membrane, or the growing foetus. Starling, however, proved that the growth is caused by a substance produced in the growing embryo. By the injection of extracts of such

* Demonstration at the Medical Society, Nov. 4th, 1908.

† Translated for THE THERAPIST from the *Berliner klin. Wochenschr.*, No. 46, 1908.

‡ *Zentralbl. f. d. gesamte Physiol. u. Pathol. des Stoffwechsels*, Nos. 5 and 6, 1907.

embryos he induced a growth in virgin rabbits similar to that found in the first phases of gestation. In conjunction with this Mamma hormon, reference may be made to the "secretine" obtained from the duodenal mucous membrane by Bayliss and Starling, which, on being intravenously injected, stimulates the pancreatic secretion in a specific way.* Mention may further be made of adrenalin, to which hormon, as one of us first demonstrated,† belongs the specific task of the mobilization of sugar. The antagonistic hormon is contained in the pancreatic extract, which, as we were able to show,‡ regulates the sugar metabolism by its antagonism to adrenalin. The examples adduced show that such very different biological functions as the growth of the breast glands, the external pancreatic secretion, and the regulation of sugar metabolism are excited and stimulated chemically, *i.e.*, by a hormon in Starling's sense emanating from certain organs which may be more or less remote in position from the organ entrusted with the particular function.

It might fairly be presumed that a similar specific hormon existed for the peristaltic action of the intestine; that is to say, that the normal intestinal peristaltic action is excited by a special hormon. By analogy with the "secretine" hormon for the pancreatic secretion, and also with the facts of the physiology of digestion discovered by Pawlow, according to which, as is well known, mastication influences the secretive action of the stomach, and the Brunner glands of the duodenum require previous secretion of hydrochloric acid by the stomach in order to be called into operation—by analogy with all these examples, which might easily be added to, it was in the highest degree probable that the place which contained the peristaltic hormon to use this convenient designation, must be the stomach. I have succeeded in producing this hormon from the

* *Journ. of Physiol.*, vol. xxviii.

† Zuelzer : *Berliner klin. Wochenschr.*, No. 16, 1907.

‡ *Deutsche med. Wochenschr.*, No. 32, 1908.

gastric mucous membrane. For obtaining this hormon it is a prerequisite—as we have already shown it to be for obtaining the pancreas hormon—that the animal should be in full process of digestion. From the empty stomach the hormon which excites the peristaltic action cannot be obtained. This hormon, like the remaining hormons, acts from within the blood circulation. If therefore the peristaltic hormon is intravenously injected into a rabbit, there appears a few seconds afterwards an energetic peristaltic process, beginning in the duodenum and continuing to the rectum. If the intestinal loop of the chloralized test rabbit is allowed to float in salt water, it will be seen how the cybala are shifted on from above downwards. First an energetic motion begins in the mesentery, which is gradually propagated towards the rectum and at last passes to the latter. Finally, the cybala and air bubbles are seen to emerge from the rectum.

As regards the mode of obtaining the hormon, it must be extracted from the gastric mucous membrane by means of (table) salt water or diluted hydrochloric acid, and the albumen removed by means of alcohol. The stomachs of the various animals (rabbits, pigs, horses, and cattle) which I tested all contain the hormon. It is interesting fact that of the four stomachs of cattle only that known as the abomasum—the fourth stomach, *i.e.*, the one charged with the work of digestion proper—contained the peristaltic hormon. It can likewise be obtained from the upper parts of the duodenal mucous membrane, though not with the same strength and regularity as from the gastric.

Starling has already pointed out (*loc. cit.*) that the action of the hormons is comparable to that of alkaloids. With peristaltic hormon the possibilities of comparison are particularly favourable, because we have in physostigmine an agent which acts on the intestinal contractions in the same way as the peristaltic hormon. One difference in the effect of these two agents may be pointed out, however, in that the peristaltic hormon brings about what is to a certain degree a physiological

course of the peristaltic action, while with physostigmine the contraction begins at the duodenum and continues to the rectum, but takes the form of a tetanic contraction, which remains as tetanus after the peristaltic wave proper has already passed.

Without going further into the clinical side, which we intend to refer to later, it may only be remarked that in some experiments we observed an immediate liquid evacuation when the peristaltic action was particularly strong. From this one may certainly infer an increased transudation, as the entire process only occupies fractions of a minute. Therefore the peristaltic hormon should be valuable for definitely clearing up the question of the action of aperients. It may also be pointed out that proof of the existence of a peristaltic hormon is calculated to modify the existing views of constipation.

CURE OF CHRONIC CONSTIPATION AND ACUTE INTESTINAL PARALYSIS WITH "PERISTALTIC HORMON."

By DR. G. ZUELZER, Berlin.*

It has been shown† that in the cells of the mucous membrane of the stomach there is produced a hormon which stimulates the peristaltic movement of the intestine in a specific manner. This hormon possesses the properties which, according to Starling, are characteristic of hormons. A hormon represents a chemical body, produced by certain groups of cells, which is carried by the blood stream to the cell complexes that are to be stimulated to specific action. Hence hormons naturally are ubiquitous, *i.e.*, in the animal organism they are present in any part reached by the blood. The possibility of demonstrating the presence of single hormons in single organs depends on the quantity of hormon contained in the respective organs, or on the precision of the methods employed. In respect of ubiquity, the hormons are like the ferments, although the latter, as products of external secretion, are not absorbed into the blood direct from the cells, but are absorbed and get into the blood passage only after being secreted.

When testing single organs for the amount of "peristaltic hormon," Dohrn, Marxer, and Zuelzer found that, with one exception, the amount of efficacious "peristaltic hormon" was so small that upon injection of the extracts of the single organ into the blood stream of the experimental animals, the intensely tonic effect exceeded by far the power of stimulating the peristalsis,

* Translated for THE THERAPIST from the *Medizinischen Klinik Wochenschrift für praktische Aerzte*, No. 11, 1910.

† Dohrn, Marxer, Zuelzer: "Spezifische Anregung der Darm-peristaltic, u.s.w." (Specific Stimulation of the Peristaltic Movement of the Intestine, &c.)—*Berl. Klin. Woch.*, No. 48, 1908.

so that, practically, those organs do not come into question as carriers of "peristaltic hormon." It was only in the spleen of all the experimental animals that we found regularly an enormous quantity of "peristaltic hormon." Here the quantity of efficacious hormon was so abundant that we have employed the spleen exclusively for the production of "peristaltic hormon" for therapeutic purposes. We felt induced to do so the more as the spleen contains hormon in a sterile medium, whereas the stomach of the experimental animals may contain tetanus bacilli or spores, the absolute removal of which presents difficulties even in the case of substances that can readily be sterilized, such as gelatine. Seeing, however, that for therapeutic purposes "peristaltic hormon" must be introduced direct into the blood stream either by intramuscular or intravenous injection, the absolutely reliable sterility of hormon is the fundamental condition of its therapeutic employment.

The demonstration of the presence of this hormon in the spleen gave rise to the question whether the spleen, in the same way as the mucous membrane of the stomach should be regarded as the place of formation or only as the storing-up organ. Hitherto we have not been able to decide this question definitely, but everything tends to show that the spleen must be regarded as being only the physiological storing-up organ for "peristaltic hormon." Further research is being made with a view of deciding this question.

With regard to the therapeutic employment of the recently discovered hormon, chronic constipation first came into consideration. It was to be applied by way of intramuscular injection. This was frequently followed by a rise in temperature (37.5° to 39° C.) of short duration, which never affected the heart (hormon fever). In most cases the local pain was but slight. Only severe cases of chronic constipation, *i.e.*, in which for several years, or even for ten years, there had been no spontaneous stool without the use of purgatives or enemas, were selected for therapeutic trial. The most

varying forms of constipation, the spastic as well as the atonic form, were indiscriminately subjected to the treatment.

I would briefly refer to the results obtained. The histories of the cases are monotonous and almost alike : for such and such a period no stool without the use of a purgative ; in some cases the patient delayed taking the remedy until subjective troubles, such as headache, appeared ; in other cases the stools were always brought on by means of castor oil, enemas, senna, &c., a few of the patients having undergone previously cures by massage, electric treatment of the intestine, but without success. The period during which the patients suffered from constipation varied between one and twenty years. Generally the troubles were slight. In most cases the psychic factor of defæcation not being spontaneous, the consciousness of being obliged to always take some remedy induced patients to give a trial to the new mode of treatment ; in other cases, headache, a feeling of discomfort, and dysmenorrhœic troubles have to be attributed to constipation.

I have carried out injections in twenty-six cases of chronic constipation. The cases in which injections were employed, in hospitals, are not included in this number. Five patients have withdrawn from observation ; in fifteen of the remaining cases a positive result was obtained ; in six cases there was no result, *i.e.*, in the fifteen cases the evacuation of the bowels has become normal subsequent to injection, and ever since takes place spontaneously and copiously once or twice daily without resort to an aperient. The effect is apparent on the second or third, sometimes on the fifth and even as late as the seventh day. At the present time the period since effecting the cures extends in some cases to a few months, in others to about six months, without relapses.

My cases are too few to admit of drawing a reliable conclusion as to why in 71 per cent. of the number a cure resulted, whereas the remedy proved ineffective in 29 per cent. After the discovery of " peristaltic

hormon'' the whole question of constipation has to be looked into afresh, and it is only on the strength of comprehensive research that one will be able to solve it. In respect of the aforesaid percentage, the fact should be taken into consideration that, with a view of arriving at an unobjectionable conclusion, I have selected only the severest cases, and that I did not prescribe any particular diet. I only advised the patients to avoid nutrients known to be conducive to constipation, such as rice, cocoa, and red wine. In order to obtain lasting results, that is to prevent the patients from relapsing into their old complaint in a shorter or longer period after the stools had become regular and spontaneous, one has, as a matter of course, to take prophylactic measures, such as enjoining patients to make sure of regularity in the evacuation of the bowels, to see to the strengthening of the abdominal muscles, to rational nutrition, &c.

Included in a special category are two cases of so-called intestinal atony (Crämer). The distinguishing feature of this complaint consists in that the patients are suffering from phenomena of intestinal fermentation, and that repeated but insufficient evacuations take place daily. In both cases the result of the injection of "peristaltic hormon" was that one sufficeint daily evacuation ensued, that the flatulence ceased, and that the condition of the clayey stools became normal. Hence it appears, as far as it is permissible to draw a conclusion from two cases, that in these cases regulation of intestinal innervation includes the principal therapeutic factor.

Now as regards the nature of the therapeutic effect, we are for the time being only able to form conjectures in this respect. Two possibilities come into consideration. The normal production of the "peristaltic hormon" is either wanting in the cases of chronic constipation, or it is insufficient in quantity; the incorporation of hormon by way of the blood passage, then, would be the stimulus for the setting in of the normal formation of hormon. Another possibility,

which appears more likely, is based on the idea that the stimulus to peristalsis is effected by the hormon by way of the nerves, that the hormon, for example, exerts a specific stimulus on the abdominal ganglia. Now in the case of chronic constipation the agent conducting the stimulus has become disturbed, in consequence, perhaps, of (auto) toxic injuries to the nervous organs, or for the reason that for a time the patient did not react on the normal stimuli. If now, by means of an inundation with artificially introduced "peristaltic hormon" a great stimulus is excreted on the nerve cells, they are again rendered capable of reacting in the old way on the normal stimuli.*

Experiments on animals having shown that intravenous injection of hormon is followed by immediate and sustained peristaltic movement of the intestine, it seemed likely that in man with acute paralysis of the intestine the use of this hormon would prove effective. In the first place there came into consideration post-operative paralysis of the intestine which hitherto defied almost any remedy, whether medicamental or mechanical. In Dr. Adler's ward at the Israelitic Hospital I had the opportunity of observing the action of hormon in a case of post-operative paralysis.

The patient, K., male, eighteen years of age, had been operated on Dec. 23rd, for gangrenous-purulent perityphlitis. On Dec. 27th, owing to symptoms of severe peritonitis, the peritoneal cavity was re-opened, and, after the discharge of copious pus, washed out with common salt, and drained. About fourteen days later the secretion had a feculent odour in consequence of the breaking through of a loop of small intestine. As the case went on, the abdomen became distended

* In proof of the fact that the curative results are not due to suggestive influence, I will quote the following passage from a letter received from Professor Alt, Uchtsprunge:—"Of ten patients (most of them epileptics and for a long period sufferers from persistent constipation) who at the Landes-Heil und Pflege Anstalt Uchtsprunge had been treated by Dr. Orland with intramuscular injections of 'peristaltic hormon,' four now have had regular evacuation for several weeks."

more and more. On Jan. 24th complete paralysis of intestine. No stool was passed from the rectum; from the perforation opening ran small quantities of feculent matter. The phenomena of paralysis increased in intensity, vomiting ensued, and the state of the patient became almost hopeless. On Jan. 27th, 15 c.cm. of "peristaltic hormon" were injected intravenously. The patient was very weak, so that in consequence of the completely prostrate action of the heart the intravenous injection could only be carried out very slowly and with difficulty. Most gentle massage carried out centralward from the place of injection, in order to mechanically move on the injection fluid, gave rise to a sanguinolent and very painful exfoliation of the skin. A few minutes after the injection there were observed on the extremely tense and previously quite motionless abdominal walls a series of peristaltic movements, which gradually increased in energy, and which about ten minutes later were demonstrable objectively through the defæcation which energetically and jerkingly set in from the intestinal fistula. The peristaltic movement continued for a few hours; then after an interval of several hours it set in again, and thence forward went on constantly. One hour after the injection slight rigor, with a rise in temperature to 38.3°C. , and slight vomiting ensued. On the following day the abdomen was considerably softer and gradually improved. On the fifth day after the injection spontaneous evacuation of the bowels per rectum ensued. The subsequent course was complicated by septic parotitis and copious diarrhœa, in consequence of which patient succumbed on Feb. 6th.

Hence in the case of this almost moribund patient with total paralysis of the intestine and loops of intestine partly agglutinated through inflammation, "peristaltic hormon" was injected intravenously, with the result that almost immediately the paralysis was permanently done away with. The by-effects of the injection were extremely slight. It seems, therefore, to be proved that in "peristaltic hormon" (which

is now made absolutely free from albumen) we possess a promptly acting and harmless remedy for combating paralysis of the intestine.

Intravenous injections were, moreover, resorted to in two other cases, the patients being inmates of the Israelitic Hospital (Dr. Adler, Prof. Blumenthal). Both cases showed similar features. In the one case a man, seventy-four years of age, about six months ago had undergone in Russia an operation of the abdomen (for reasons not ascertainable); the other, a man of sixty-seven, had in November been operated successfully for carcinoma of the rectum. Both patients had had no stool for nine days. The use of glycerine enemas and castor oil had proved ineffective in both cases. In neither of them was it possible to decide in a differential diagnostic manner whether it was a question of a volvulus (which not infrequently exists in cases of tumour of the intestine) or of a solid occlusion of the intestine by the tumour. In the case of the first patient an injection of 16 c.cm. of "peristaltic hormon" was followed by the setting in of peristaltic movement, which by way of auscultation was ascertainable owing to rumbling sounds. About twelve hours after the injection a very copious evacuation of the bowels took place spontaneously. Two days later castor oil was administered once more with the result that further large quantities were evacuated, so that soon after the patient could be discharged, free from trouble. The injection had been followed by a slight rise in temperature to 38.4° C., without rigour. Other disagreeable symptoms were not noticed.

In the case of the second patient, however, the injection of 15 c.cm. effected only the appearance of a pronounced peristaltic but unsettled movement, which lasted till the next day, was ascertainable by auscultation and was accompanied by flatulence and the passage of small quantities of faecal matter. The highest temperature was 38.2° C. An evacuation proper of the bowels did not ensue, but the circumference of the distended abdomen visibly diminished, and a distinct stiffening

of the part of the intestine situated in front of the obstruction became manifest, so that the tumour could be localized beyond doubt. On the following day the patient was provided with an anus præternaturalis. In the further course of the complaint the surgeon was struck with the extraordinarily good and copious stools, which favoured the curative process.

It is instructive to consider these two cases which came under treatment at the same time. It shows, firstly, that the intravenous injection, well tolerated as it was by two senile patients, is a perfectly harmless therapeutic measure. It shows, moreover, that the stimulation of the peristaltic movement is so gentle that even in the case of organic occlusion it does not lead to severe disturbances. On the other hand, it may claim attention as a differential diagnostic aid because, as is shown by the first case, it saved the patient an otherwise unavoidable operation, which, no doubt, might have turned out disastrous.

Future experience will disclose whether a negative result after an intravenous injection of "peristaltic hormon" is in diagnostic respects a proof of the existence of organic stenosis, and whether it speaks clearly against the existence of paralytic or dynamic ileus; furthermore, whether in cases of slight axis rotation it is possible to do away with it by inducing regulated peristaltic movements.

NOTE.--In the meantime "peristaltic hormon" has been injected in four other instances without being followed by any by-effects other than a slight rise in temperature and a light attack of rapidly disappearing nausea, accompanied by slight vomiting, in a case of carcinoma of the stomach.

ON ZUELZER'S "PERISTALTIC HORMON."

By DR. SAAR, Berlin (Staff Physician and Clinical Assistant at the Second Medical University Clinic of the Charité Hospital. Director: Privy Councillor Prof. Kraus).*

SOME clinical observations which I made in 1909 with Zuelzer's peristaltic hormon on a few patients in our clinic are briefly communicated below.

The preparation was first employed only in cases in which no result, or no permanent result, was obtainable by the usual methods of treating chronic constipation. By chance the very first case in which we used the hormon was an entire success. The patient was a builder, fifty-seven years of age, who attended the Charité Hospital on Dec. 28th, 1908, on account of pains in the chest (right side), cough, and mucous expectoration, accompanied by constipation and loss of appetite. A point worth noting in the previous history was that he had suffered from lead poisoning for six weeks in 1880, with severe abdominal pains and constipation for days. The clinical diagnosis was: Tuberculous affection of the left apex, pleural induration on the right side below. Arteriosclerosis in a moderate degree. The achylia gastrica explained the dyspepsia. Dietary directions were given for the constipation. Castor oil and afterwards podophyllin were used without success. Only by regular oil clysters administered late in the evening and kept during the night was a stool obtained. When the oil clysters were stopped for trial the constipation immediately re-appeared.

We therefore determined in this case to make use of the hormon treatment, as a lasting result was not effected with four weeks of the oil cure.

* Translated for THE THERAPIST from *Medizinische Klinik*, No. 11, 1910.

On the morning of Feb. 6th, 1909, the patient was given an intramuscular injection of 20 c.cm. peristaltic hormon in the gluteal region. The temperature rose to 39.1° C., and a sensation of heat, body fatigue, and some headache appeared. Three or four hours after the injection he stated that "his stomach was rumbling so," and there was a marked expulsion of intestinal gases. In the afternoon the peristaltic disturbance had abated, but no evacuation had taken place. As an "agent of dislodgment," so to speak, two tablespoonfuls of castor oil were given. Some hours later an ample, well-formed stool was discharged.

The interesting feature in this case is that, without any further aid and without any alteration in diet, the patient for ten days had an evacuation twice a day without trouble, from the following day onwards. At the same time the appetite increased, the general condition became excellent, and the patient himself could not say enough in praise of this aperient. On Feb. 20th, he left the clinic as cured, but attended several times during the following months, always reporting that he no longer had any difficulties.

A second case related to a farmer, sixty-one years of age, who, owing to difficulty of evacuation, attended the Charité on July 17th, 1909.

The patient had a somewhat enlarged liver and abdominal distension by gas. He complained of frequent but inoffensive eructation. The evacuations had stopped since the end of June. Treatment by diet and aperients hitherto without result. Examination of the stomach showed normal acid values and regular motility. Nothing abnormal found from the rectum onwards. Carlsbad salts and flushing the stomach did not relieve the troubles. Castor oil proved a good aperient, but caused abdominal pain. On July 29th, an injection of 15 c.cm. peristaltic hormon was made into the gluteal muscles. There was no rise of the body temperature afterwards, but only shivering and discomfort on the night after the injection, which disappeared on the following day.

The treatment proved successful, with regular evacuation from July 30th. No further difficulty from meteorism. The patient left the clinic on July 31st, 1909. He informed us by letter on Sept. 15th, 1909, *i.e.*, six weeks after the injection, "that the medicine you used in my case has had a lasting good effect. I at first continued to take a little Carlsbad salts [prescribed for the stomach distension]. I now no longer need any medicine. I am now perfectly cured and healthy," &c.

The third case, an estate manager, thirty-three years of age, was transferred to the Clinic on Nov. 4th, 1909, by the Grabowsee Lung Institute for treatment of obstipation. Had been in Grabowsee since Aug. 21st, 1909, with pulmonary tuberculosis, and at the end of September marked constipation set in for several days. Evacuation had again ceased since Oct. 23rd. Notwithstanding the use of the most various drugs and physical and dietetic measures, evacuation of the bowels had only taken place twice during the last fourteen days. Examination showed, in addition to tuberculosis and a slight inflammation of the kidney, the stomach to be a little distended, but not tender; colon descendens contracted in the left lower hypogastric region and felt to be empty through the abdominal walls. Belladonna plugs and oil clysters had no effect. On Nov. 7th, intramuscular injection of 15 c.cm. of peristaltic hormon. In the evening some peristaltic disturbance. Administration of three tablespoonfuls of castor oil emulsion as an "agent of dislodgment." On the night following, abundant stool. On the morning of Nov. 8th, temperature 38.4° C., pulse 105; evening, 38.3° C. General condition very slightly deranged. On Nov. 9th, morning, 36.8° C., pulse 90, again good evacuation. From then until discharged on Nov. 13th, regular evacuation without any further treatment. On Dec. 2nd, 1909, we received a written communication from the patient in Grabowsee: "I am glad to inform you that evacuation of the bowels continues to be quite regular and normal, without the use of any aperient," &c.

If we glance over the three case histories indicated above, we are first struck by the effect resulting from a single administration of the peristaltic hormon. It is as though a stationary pendulum had been set going regularly by a single push. In regard to suggestions which may result from our hitherto limited practical experience, I would emphasize the fact that it is advisable to make the injection in the early morning, in order to allow the temperature reaction which mostly follows to subside during the day. We would also point to the administration of an "agent of dislodgment" in the form of a single ample dose of emulsio ricinosa.

It cannot of course be said with absolute certainty which cases of obstinate constipation are best adapted for hormon treatment. We have already had a few failures to record. I would mention an old arteriosclerotic patient, in whom the cybala were lodged in the sigmoid flexure, evacuation being only obtainable by clysters. Here two doses of peristaltic hormon failed. Nevertheless the action of the preparation in the few cases observed by us is such that it must be regarded as an interesting and grateful task of clinical investigation to make further experiments on an extended scale.

THE APPLICATION OF PERISTALTIC HORMON (HORMONAL) IN SURGERY.

By Prof. DR. A. HENLE, Dortmund.*

IN 1902 Vogel recommended physostigmine in doses of 1 mg., subcutaneously injected, for improving intestinal peristalsis after operation. Although one may approve of the indications fixed by Vogel, it should not be overlooked that the remedy recommended by him cannot possibly be considered as certain and trustworthy.

Heubner especially points out that the improving effect on the intestines of physostigmine in subcutaneous applications of 1.0 to 1.2 mg. set in in some persons, whilst in others it failed entirely. As, furthermore, the injections were accompanied by nausea, Heubner believes that a practical application of the remedy is impossible.

In my own experiments I may say shortly that the remedy failed in several cases ; and that I often further observed in conjunction with the injection severe, although temporary, collapse.

As my experiments with physostigmine did not lead to satisfactory results, the notices of another new physiological remedy, named peristaltic hormon (Hormonal), the specific properties of which lie in the improvement of peristalsis, were of great interest to me.

In referring to the scanty literature on this remedy (Zuelzer, Dohrn, Marxer, and Saar), I only wish to mention that under the collective name of "hormon," according to the work of Starling, should be placed those chemical bodies which, when set free internally from certain organs during their action, are carried to other organs in order to incite these to work, so that the activity of the one brings about that of the second organ in a chemical way.

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The peristaltic hormon in question is produced, as Zuelzer, Dohrn, and Marxer have proved, by the stomach and upper duodenum in the course of the digestive process, and can be prepared from the respective mucous membrane. When injected directly into the blood circulation of an experimental animal it causes a most remarkable peristaltic wave, which commencing at the duodenum goes right up to the rectum, and terminates with the excretion of fæces or gas from the anus. The intestinal peristalsis joins therefore the stomach digestion in a very suitable way for the transmission of the ingesta.

In examining the various organs for a probable contents of peristaltic hormon, the three authors found that it is contained in the spleen in large quantities, so that probably this organ may be regarded as a storing place for this product produced in the stomach.

For obvious reasons the peristaltic hormon was prepared from the spleen only, which, contrary to the stomach, produces no difficulties in the way of asepsis in obtaining the medium.

The remedy is produced in sterile form by the Chemische Fabrik auf Actien (vorm. E. Schering), Berlin, and is sold in bottles of 15 c.cm. [in future, in bottles of 20 c.cm.—Editor]. If a quick effect is desired one injects the 15 c.cm. intravenously; in less acute cases intramuscular injection of the total contents of the bottle suffices. For the latter purpose the manufacturers add a little Eucaine to the product in order to avoid muscular pain.

No by-effects after the injections, except short temporary advances of temperature (37.5° to 39° C.) were observed. No heart troubles.

The experiences which have been published so far refer generally to cases of chronic constipation, and the prospect appears to be very promising for the combating of this trouble. The outstanding fact is, that after one single injection the constipation disappears for weeks, or perhaps months, and not as with purgatives, when only a single motion takes place.

Zuelzer mentions three acute cases treated with peristaltic hormon. The first case was that of a patient with a paralyzed ileum, the result of suppurative peritonitis after appendicitis. An intestinal fistula formed. A few minutes after the intravenous injection peristaltic movement of the stomach walls, which were strained to the maximum, could be observed, and after ten minutes commenced an energetic defæcation from the fistula. During the next day a natural motion took place, but the patient, after the occurrence of septic parotiditis and severe diarrhœa, died of exhaustion.

In the other two cases, aged men, no motion had taken place for nine days. In both glycerine enema and castor oil had been given without any success.

In one case peristalsis set in shortly after the intravenous hormon application, with a large motion twelve hours afterwards. In the other case also pronounced peristalsis occurred, increasing to intestinal stretching, which proved the presence of an organic obstruction in form of cancer recrudescence. Cure after application of an anus preternaturalis.

It appeared desirable to extend the experiments in the direction of acute paresis and paralysis of the intestines. Hence I applied Hormonal in a number of cases, and I wish here to mention (I intend to give a more detailed report later) that the experiences obtained were most encouraging as to further application of the remedy. I give a brief account of two cases, as they seem to point most obviously to the effect of the remedy.

The first case is somewhat similar to the first of Zuelzer's cases.

Woman, fifty-two years of age, with peritonitis for two days, who complained suddenly of pains. Neither motion nor flatulence. Patient looked very much run down, was somewhat lethargic. Pulse 160, very low. Abdomen greatly dilated and everywhere susceptible to pressure. In the depending parts, drum-like sounds when tapping. Peristalsis not noticeable even auscultatorily.

The relatives, to whom I gave the hopeless prognosis, desired operative assistance. I decided to try it (1) with an adrenal-salt infusion; (2) camphorated oil douches of the abdominal cavity; (3) with Hormonal. The latter was given in quantities of 15 c.cm. mixed with the infusion solution. In the abdominal cavity an abundance of serous purulent exudation with marked addition of gall pigment. Fibrinous layers on the intestines. The sphere of the appendix free. Carcinomatous knots in liver. Exudation removed as far as possible. 100 c.cm. 1 per cent. camphorated oil given per clyisma and thereby distributed. Iodoform gauze bags in the abdominal cavity; partly closing of wound. The pulse scarcely improved after the enema. After close of operation increased flatulence prevalent, with simultaneous slight quantity of diarrhoeic motion. Half an hour afterwards lethal exitus. The post-mortem showed perforated gall cancer. *Bacterium coli* produced from pus.

I believe that in this case the Hormonal injection in the apparently quite paralytic intestine produced contraction, and may remark that this was no pseudo result, as is produced sometimes in laparotomies by pressure on the exposed large intestine, for motion and flatulence occurred only after the reposition of the intestines and after closure of the intestinal cover. After this experiment I believe that by the combined application of Hormonal intravenously with a simultaneous application intra-abdominally of camphorated oil, sometimes a case of peritonitis otherwise hopeless may be saved.

A second case was more successful. Here we had to deal with gallstone ileus, which I operated on July 3rd, 1910, at noon on the fourth day of its existence. The patient was a woman, fifty-eight years of age, rather stout. Painful attack some seven or eight years ago, which was declared to be gallstone colic. Since June 29th, neither motion nor flatulence. Repeated vomiting, fecaloid since July 1st. Physostigmin (1mg.) was given externally, without result. Temperature under 37°C.,

pulse 80. Abdomen uniformly but not severely strained. Peristalsis proved on auscultation. Sounds not resonant. No stiffening. In the urine an abundance of indican. The laparotomy showed an oval-formed stone weighing 47 grms., size 8.5 by 3.5 cm., which evidently filled the gall bladder, and which moved through the perforation into the intestines. The firmly settled stone was moved an inch upwards into the enlarged intestine and taken out by longitudinal section. The wound was closed by three rows of rectilinear stitches. To avoid any unnecessary injury of the intestines, only that part of the intestine holding the stone was eventrated, hence it could not be ascertained to what height the closing had taken place. Abdomen stitched. During the following night fecaloid vomiting. July 4th, meteorism stronger. Noise in the intestines distinguishable. In douching the intestines a little wind escaped. Towards the evening greater vomiting. Stomach washing produced more fecaloid liquid. The general condition deteriorating. The pulse became weaker. Intestinal washing unsuccessful. In the evening at 6.30, 15 c.cm. Hormonal intravenously. Up to 10 o'clock increasing collapse. During the first half of the night distinctly noticeable noises in the intestines. During the latter part of night marked flatulence. July 5th, in the morning, again vomiting of small quantities of fecaloid liquid. Afterwards no more vomiting. After a spoonful of castor oil, a small thin motion. During the following days spontaneous discharge of wind. Intestinal washing twice daily produced slight amount of motion. July 6th, after oil enema, abundant motion. Convalescence was retarded by heart weakness, loss of appetite, and bronchitis, but on the sixteenth day the patient was dismissed as cured.

Although generally in cases like those described here the *post hoc* is difficult to distinguish from the *propter hoc* so far as the applied therapy is concerned, I must consider the developement as a sure success of Hormonal.

The appearances of intestinal paralysis were in rapid progress during the day after the operation. Noise in the intestines could not be heard. Three hours after the Hormonal injection the intestines commenced to work again, and after further three hours marked discharge of wind. With the starting of peristalsis the increasing deterioration stopped, to give way to improvement. I do not hesitate in saying *Hormonal saved the patient's life*.

I have further applied Hormonal in a number of post-operative partly severe intestinal pareses, and as it appears to me with good success. Generally after six to eight hours flatulence took place spontaneously, or after glycerine enema or intestinal lavage, whilst these remedies previously failed completely. Twice in adhesive peritonitis after laparotomy Hormonal injections intravenously were made immediately after the operative removal of in-growth. Here also peristalsis soon set in, and flatulence quickly followed.

Naturally in these cases, which probably without Hormonal would have overcome their intestinal paresis, it is difficult to ascertain how far the above-mentioned remedy brought about a change for the better or accelerated it. I believe, however, in accordance with earlier publications and my own experience, that Hormonal is a remedy of great value for the physiological intestinal movement, and in abdominal surgery I believe it to be of eminent importance.





